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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,616	01/22/2004	Luisa Hernandez-Ramirez	91349	5023

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EXAMINER	
SIMMONS, CHRIS E	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,616	HERNANDEZ-RAMIREZ ET AL.	
	Examiner	Art Unit	
	CHRIS E. SIMMONS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,13 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,13 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/04/2010 has been entered.

Applicants' arguments, filed 06/04/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Applicant's arguments, see page 5, 5th sentence, filed 06/04/2010, with respect to the rejections of claims 1, 13, 15, 17, 19 and 21 under 35 USC 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the each drug already being known to treat infections that concurrently occur.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 13 and 17- 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. (Clin. Lab. Med.(1989 Sep); 9(3):525-33) in view of Sobel et al. (AM J Obstet Gynecol(1995 Apr); 172(4 Pt. 1):1263-8) and Gillis et al.

(Drugs(1996 Apr);51(4):621-38), the combination taken further in view of Gennaro, Alfonso. (Remington's pharmaceutical Sciences. Easton, PA:Mack Pub. Co., 1990) ("Remington's").

Spielberg discloses the most common cases of vaginitis/vaginosis are caused by yeast (predominantly Candida albicans), the protozoan Trichomonas vaginalis, or a specific mixture of bacteria (bacterial vaginalis). It is not uncommon for a woman to have more than one microbial source for her vaginal signs and symptoms. A vaginal examination should include appropriate test for detection of all three of these agents. Because vaginitis/vaginosis cannot be adequately diagnosed solely on the basis of physical exam and symptoms, some laboratory work is required. The reference does not expressly teach a single tablet comprising a uniform mixture of fluconazole and either tinidazole or secnidazole.

Sobel discloses Candida vaginitis is safely and effectively treated by a single dose of 150 mg oral fluconazole. See abstract. The reference does not expressly teach a single tablet comprising a uniform mixture of fluconazole and either tinidazole or secnidazole.

Gillis teaches bacterial vaginosis or vaginitis is effectively treated with a single 2g dose of secnidazole or with a single dose of 2g of tinidazole (See Figure 4 at page 633). The reference does not expressly teach a single tablet containing both fluconazole and tinidazole or secnidazole.

Remington's disclose drug substances are most frequently administered orally by means of solid dosage forms such as tablets and capsules. Production methods

require other ingredients in addition to the active ingredients. Additives may be added in order to improve appearance, stability and aid in disintegration after administration. See page 1633, 1st paragraph. Tablets remain popular as a dosage form because of the advantages afforded both to the manufacturer (e.g., simplicity and economy of preparation. stability and convenience in packaging, shipping and dispensing) and the patient (e.g., accuracy of dosage, compactness, portability, blandness of taste and ease of administration). See *Id.,* 1st paragraph under *'Tablets'.* Microcrystalline cellulose is usually used as an excipient in direct compression formulas, i.e., tablet formulations. See Remington's page 1634, 2nd column, 2nd full paragraph. Compression equipment continued to improve both as to production speed and the uniformity of tablet compressed. See Remington's page 1633, 2nd column under *'Tablets'*, 1st full sentence. Content uniformity is important to ensure that each tablet has the same amount of active agent dose. See page 1640, 2nd column, 1st full paragraph. Remington's does not expressly teach a single tablet containing fluconazole and secnidazole or tinidazole.

Since it is not uncommon for a woman to have more than one microbial source (e.g., Candida, bacteria, and trichomonas) for her vaginitis/vaginosis symptoms (see Spielberg), the skilled artisan would be motivated to treat the woman with an oral combination of agents such as fluconazole and tinidazole or fluconazole and secnidazole since the oral fluconazole is known to treat Candida infections and both oral tinidazole and oral secnidazole are known to treat Trichomonas and bacterial vaginal infections – all of which are the most common causes of vaginitis/vaginosis (see Spielberg). Because it will take additional time for the required laboratory results (see

Spielberg) to pinpoint the actual cause of the symptoms, one of ordinary skill in the art would especially be motivated to treat the woman with the aforementioned combination early in the treatment schedule to provide broad protection from the most common causes of vaginitis/vaginosis, i.e., candidiasis, Trichomoniasis and bacterial vaginosis (see Spielberg).

One of ordinary skill in the art would have found it obvious to make a single uniform oral tablet (see Remington's) containing fluconazole (see Sobel) and tinidazole or secnidazole (see Gillis) for the treatment of women presenting with vaginitis/vaginosis because uniform tablets are a commonly used oral dosage form and is well within the skill of one of ordinary skill in the art as the principles are described in Remington's. The motivation to make a single tablet would be to provide easier administration of both active ingredients.

With regards to the amounts of each of fluconazole and secnidazole or tinadazole recited in the claims, it is noted that the combination of the disclosed amount of fluconazole taught by Sobel (150mg) and the disclosed amounts of secnidazole (2g (2000mg)) and tinidazole (2g (2000mg)) taught by Gillis are within the claimed ranges of claims 1- 3 and 13 (note: 150mg fluconazole : 2000mg secnidazole/tinidazole is 7% : 93%).

It is noted that claims 17-22 define concentrations of each agent which fall slightly below the amounts taught as effective by Sobel and Gillis; however generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is

critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. MPEP 2144.05 [R-5] IIA. In this case, the combination of all the ingredients are suggested in the prior art, i.e., the general conditions are disclosed. The only difference between the prior art and the current claims is the concentrations disclosed. Since there is no evidence of the criticality of these concentrations, their differences from the prior art is not enough to render the claims patentable over the prior art.

Claims 1, 13, 17, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. (Clin. Lab. Med.(1989 Sep); 9(3):525-33) in view of Sobel et al. and Wallin et al. (Cited in 09/02/2009 Office action), the combination taken further in view of "Remington's".

The disclosure of Spielberg, Sobel and Remington's are described above. The references do not teach tinidazole.

Wallin et al. discloses of tinidazole is an effective antimicrobial at 2 grams and 1.6 grams. A single oral dose offers a potent and practical way to treat T. vaginalis (p. 150, *Summary)*. Wallin does not expressly teach a combination of fluconazole with tinidazole.

Since it is not uncommon for a woman to have more than one microbial source (e.g., Candida, bacteria, and trichomonas) for her vaginitis/vaginosis symptoms (see Spielberg), the skilled artisan would be motivated to treat the woman with an oral combination of agents such as fluconazole and tinidazole since oral fluconazole is known to treat Candida infections and oral tinidazole is known to treat Trichomonas infections. Because it will take additional time for the required laboratory results (see Spielberg) to diagnose the actual cause of the vaginal symptoms, one of ordinary skill in the art would especially be motivated to treat the woman with the aforementioned combination at least as an initial treatment to provide broader protection from the most common causes of vaginitis/vaginosis, i.e., candidiasis and Trichomoniasis (see Spielberg).

One of ordinary skill in the art would have found it obvious to make a single uniform oral tablet (see Remington's) containing fluconazole (see Sobel) and tinidazole (see Wallin) for the treatment of women presenting with mixed vaginitis/vaginosis because uniform tablets are a commonly used oral dosage form and is well within the skill of one of ordinary skill in the art as the principles are described in Remington's. The motivation to make a single tablet would be to provide easier administration of both active ingredients.

With regards to the amounts of each of fluconazole and tinadazole recited in the claims, it is noted that the combination of the disclosed amount of fluconazole taught by Sobel (150mg) and the disclosed amounts of tinidazole (2g) taught by Wallin are within

the claimed ranges of claims 1 and 13 (note: 150mg fluconazole : 2000mg tinidazole is 7% : 93%).

It is noted that claims 17, 19 and 21 define concentrations of each agent which fall slightly below the amounts taught as effective by Sobel and Wallin; however generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. MPEP 2144.05 [R-5] IIA. In this case, the combination of all the ingredients are suggested in the prior art, i.e., the general conditions are disclosed. The only difference between the prior art and the current claims is the concentrations disclosed. Since there is no evidence of the criticality of these concentrations, their differences from the prior art is not enough to render the claims patentable over the prior art.

Claims 2, 3, 18, 20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al. and Videau et al. (Cited in 09/02/2009 Office action), the combination taken further in view of “Remington’s”.

The disclosure of Spielberg, Sobel and Remington’s are described above. The references do not teach tinidazole.

Videau et al. discloses 2 grams of secnidazole are effective for the antimicrobial treatment of vaginal infection (p. 78, *Table 1).* Videau does not expressly teach a combination of fluconazole with secnidazole.

Since it is not uncommon for a woman to have more than one microbial source (e.g., Candida, bacteria, and trichomonas) for her vaginitis/vaginosis symptoms (see Spielberg), the skilled artisan would be motivated to treat the woman with an oral combination of agents such as fluconazole and secnidazole since oral fluconazole is known to treat Candida infections and oral secnidazole is known to treat Trichomonas infections. Because it will take additional time for the required laboratory results (see Spielberg) to diagnose the actual cause of the vaginal symptoms, one of ordinary skill in the art would especially be motivated to treat the woman with the aforementioned combination at least as an initial treatment to provide broader protection from the most common causes of vaginitis/vaginosis, i.e., candidiasis and Trichomoniasis (see Spielberg).

One of ordinary skill in the art would have found it obvious to make a single uniform oral tablet (see Remington's) containing fluconazole (see Sobel) and secnidazole (see Videau) for the treatment of women presenting with mixed vaginitis/vaginosis because uniform tablets are a commonly used oral dosage form and is well within the skill of one of ordinary skill in the art as the principles are described in Remington's. The motivation to make a single tablet would be to provide easier administration of both active ingredients.

With regards to the amounts of each of fluconazole and secnidazole recited in the claims, it is noted that the combination of the disclosed amount of fluconazole taught by Sobel (150mg) and the disclosed amounts of secnidazole (2g (2000mg)) taught by Videau are within the claimed ranges of claims 2 and 3 (note: 150mg fluconazole : 2000mg secnidazole is 7% : 93%).

It is noted that claims 18, 20 and 22 define concentrations of each agent which fall slightly below the amounts taught as effective by Sobel and Videau; however generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. MPEP 2144.05 [R-5] IIA. In this case, the combination of all the ingredients are suggested in the prior art, i.e., the general conditions are disclosed. The only difference between the prior art and the current claims is the concentrations disclosed. Since there is no evidence of the criticality of these concentrations, their differences from the prior art is not enough to render the claims patentable over the prior art.

Claims 6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Gillis et al., and "Remington's", the combination taken in view of USP 5,660,860.

The disclosures for Spielberg, Sobel, Gillis, and "Remington's" are described above. The references do not expressly disclose the vehicle ingredients in the claims.

The '860 patent discloses optionally coated water-dispersible tablets to provide a tablet which is capable of dispersing in water within 3 minutes. The composition comprises inert ingredients such as microcrystalline cellulose, sodium glycolate of starch, polyvinylpyrrolidone, magnesium stearate and white opadry (abstract; claim 16). The reference does not disclose fluconazole and either tinidazole or secnidazole.

It would have been obvious to one of ordinary skill in the art to add the vehicle ingredients microcrystalline cellulose, sodium glycolate of starch, polyvinylpyrrolidone, magnesium stearate and white opadry described in the patent to the fluconazole and tinidazole or fluconazole and secnidazole oral tablet compositions suggested by the other references. The motivation for doing so would have been the desire to make a water dispersible tablet which is capable of dispersing in water within a short period of time as described in the patent.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Wallin et al., and "Remington's", the combination taken in view of USP 5,660,860.

The disclosures for Spielberg, Sobel, Wallin, and "Remington's" are described above. The references do not expressly disclose the vehicle ingredients in the claims.

The '860 patent discloses optionally coated water-dispersible tablets to provide a tablet which is capable of dispersing in water within 3 minutes. The composition comprises inert ingredients such as microcrystalline cellulose, sodium glycolate of starch, polyvinylpyrrolidone, magnesium stearate and white opadry (abstract; claim 16). The reference does not disclose fluconazole and tinidazole.

It would have been obvious to one of ordinary skill in the art to add the vehicle ingredients microcrystalline cellulose, sodium glycolate of starch, polyvinylpyrrolidone, magnesium stearate and white opadry described in the patent to the fluconazole and tinidazole oral tablet compositions suggested by the other references. The motivation for doing so would have been the desire to make a water dispersible tablet which is capable of dispersing in water within a short period of time as described in the patent.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spielberg C.A. in view of Sobel et al., Videau et al., and "Remington's", the combination taken in view of USP 5,660,860.

The disclosures for Spielberg, Sobel, Videau, and "Remington's" are described above. The references do not expressly disclose the vehicle ingredients in the claims.

The '860 patent discloses optionally coated water-dispersible tablets to provide a tablet which is capable of dispersing in water within 3 minutes. The composition comprises inert ingredients such as microcrystalline cellulose, sodium glycolate of

starch, polyvinylpyrrolidone, magnesium stearate and white opadry (abstract; claim 16). The reference does not disclose fluconazole and secnidazole.

It would have been obvious to one of ordinary skill in the art to add the vehicle ingredients microcrystalline cellulose, sodium glycolate of starch, polyvinylpyrrolidone, magnesium stearate and white opadry described in the patent to the fluconazole and secnidazole oral tablet compositions suggested by the other references. The motivation for doing so would have been the desire to make a water dispersible tablet which is capable of dispersing in water within a short period of time as described in the patent.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS E. SIMMONS whose telephone number is (571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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